Remarks

The present claims have been amended to more clearly state that which applicants believe to be their invention, and to claim additional embodiments of the invention. More particularly, the claims have been amended to clarify objected terminology, to make antecedent language consistent, and to add new claims 38-42. Support for new claim 38 is found on page 19, lines 19-21 and for new claims 39-42 on page 11, lines 10-24, and page 16, lines 20-24.

Claims 1-3, 5-7 and 9-19 stand rejected under 35 USC § 112, second paragraph as being indefinite. The Examiner has objected to claims 1 and 19 as lacking antecedent basis and for being vague for the use of the term "the S19 monoclonal antibody". The objected terminology has been removed from the claims rendering the objection moot. The Examiner has also objected to claim 9 stating that it is not clear for what the composition is active. Applicants have amended claim 9 to remove the objected language rendering the objection moot. Claim 18 has been amended to delete the objected term "the presence" and to add a step of identifying sperm immobilized on the solid support (support found on page 16, line 29-page 17, line 2). The amendment to claim 18 is believed to fully address the Examiner's objection. The amended claims are believed to fully comply with the requirements of 35 USC § 112, second paragraph and applicants respectfully request the withdrawal of the rejection of claims 1-3, 5-7 and 9-19 under that statutory section.

Claims 1-3, 7, 9-12, 15-19 and 33-36 stand rejected under 35 USC § 103, as being unpatentable over Herr et al., (US 5,830,472) in view of Owens et al., (J. Immunol. Meth. 168: 149, 1994). Applicants respectfully traverse.

Firstly, applicants note that the claims have been amended to clarify that the invention is directed to a single chain antibody, wherein the antigen-binding region has been specifically identified by sequence. The references cited by the Examiner fail to provide any teaching regarding the selection of the specific sequences that were used to construct the claimed single chain antibody of the present invention. Although the general procedures for preparing antibodies and recombinant derivatives thereof are known, "obvious to try" is not the standard under which obviousness can be established, especially in the arts relating to the

preparation of antibodies (see Ex parte Old 229 USPQ 196 (BPAI 1985). The teachings provided by the cited references are merely an invitation to experiment and fail to teach or suggest the specific single chain antibody that applicants have constructed and now claim as their invention.

Attached as Appendix A is a comparison of the sequences of the heavy chain and light chains as disclosed in Herr et al. (designated as the "'472 patent"), with the actual sequences (designated as the "present") used to form the single chain antibodies of the present invention. In addition to the many nucleotide sequence differences (a total of 31) between the Herr et al. disclosed sequences and those used in the claimed single chain antibody, only a portion of the S19 heavy chain was used, and the S19 light chain as disclosed in the Herr reference contains a serious error that would result in a frameshift in the expressed sequence. The Examiner discounts the significance of the prior art sequencing errors by noting that the S19 hybridoma is deposited and readily available. However, the skilled practitioner would have no reason to anticipate that the sequences were in error and would instead rely on the teachings provided by the cited references.

The lack of any guidance that the previously disclosed sequence of Herr et al. contains errors, in addition to the lack of any teaching regarding the selection of the sequences to use to prepare an effective single chain antibody, casts doubts on the ability of a skilled practitioner, using the knowledge that was available at the time, to do what applicants have done and now claim as their invention. Applicants respectfully submit the contention that skilled practitioners would correct an error in the sequence that they were not aware of is impermissible hindsight reconstruction. It was applicants' discovery of the sequencing errors and the identification and selection of the necessary elements of the S19 sequence for creation of the single chain antibody that resulted in a functional single chain antibody. Furthermore, these shortcomings of the Herr reference are not remedied by the teachings of the Owens reference. Owens simply provides general teachings regarding the preparation of recombinant antibodies.

In addition, the cited references fail to provide any motivation for preparing the single chain antibodies of the present invention. The Examiner contends that Herr et al

directly suggests making recombinant antibodies and that this in combination with the benefits taught by Owens would make the present invention obvious. Applicants respectfully traverse, noting that while Herr et al. suggests the possibility of making recombinant antibodies, the reference is devoid of any suggestion relating to the synthesis of single chain antibodies. Furthermore, as clearly indicated by the Owens et al. there is a great variety of different recombinant antibody types that can be made to "capture the benefits of stability, higher yield and/or lower production costs":

> The preparation of homogenous antibody fragments by enzymatic digestion can be difficult and often conditions have to be optimized for each antibody. By contrast, recombinant DNA technology can be used to produce defined fragments of any immunoglobulin for study, e.g., recombinant Fab fragments ..., recombinant Fc fragments... and recombinant Fvs .... (page155)

Therefore a reading of the Herr and Owens references provides no motivation to specifically make a single chain antibody derivative of S19 as applicants have done and now claim as their invention. Moreover the Owens reference actually discourages the preparation of single chain antibody derivatives, and thus teaches away from the present invention. See page156:

> However, many antigen-antibody interactions involve both combining sites of the antibody either in binding to a molecule with more than one antigenic determinant or in bridging two separate cell surface molecules. Therefore, the monvalent binding of sFvs [single chain antibodies] may limit their effective use. This is indicated by the following two studies.

Surprisingly, as noted on page 17, lines 27-28 of the present application, the claimed single chain antibodies of the present invention are capable of forming multimers that are able to agglutinate sperm cells. Such a result is contrary to the teachings of Owens and this unexpected result enhances the utility and desirability of the claimed single chain antibodies.

Simply stated the Herr et al. and Owens et al. references fail to provide the motivation to make a single chain antibody derivative of the S19 antibody nor do they provide

an adequate teaching of how to make the presently claimed single chain antibodies. Applicants respectfully submit the claimed invention, as amended herein, is nonobvious over the teachings of the Herr et al. and Owens et al. references and applicants request withdrawal of the rejection of the claims under 35 USC § 103.

Claims 5, 6, 13 and 14 stand rejected under 35 USC § 112, first paragraph for lack of enablement and failure to meet the written description requirement. The Examiner contends that the specification fails to provide any guidance of how to prepare antibody conjugates or how one would administer such compositions. Applicants respectfully traverse.

Applicants note that the written description does not require applicants to include information that is well known to those skilled in the art. The prior art is replete with examples of how to conjugate antibodies to molecules useful as labels in detection assays and effector molecules such as heterologous polypeptides, drugs, radionuclides, or toxins. See, e.g., PCT publications WO 92/08495; WO 91/14438; WO 89/12624; U.S. Pat. Nos. 5,314,995 and 6,475,753; and EP 396,387. One of ordinary skill would readily appreciate from applicants' disclosure that applicants were in possession of the claimed invention.

Claims 5, 6, 13 and 14 are original claims and applicants note that in the Revised Interim Guidelines For Examination of Patents Applications Under 35 USC § 112, first paragraph, issued by the US Patent and Trademark Office (64 Fed. Reg. 71427, 1999), the Guidelines state that rejection of an original claim for lack of written description should be rare. In light of the public knowledge at the time of the present invention, regarding the preparation and use of antibody conjugates, applicants respectfully submit that the Examiner has failed to meet his initial burden of establishing why one of ordinary skill in the art would not recognize applicants' written description as providing adequate support of the claims.

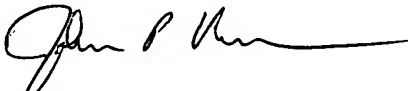
The Examiner has also rejected the claims for lack of enablement. Again, applicants respectfully submit that one of ordinary skill could prepare the single chain antibodies of claims 5, 6, 13 and 14 based on the disclosure of the present invention and the knowledge of the skilled practitioner. The Examiner's rejection appears to center on his contention that applicants have failed to adequately teach a method of using these compounds *in vivo*. However, applicants are not claiming an *in vivo* method. While the antibody

conjugates of the present invention may have various diagnostic and contraceptive uses, applicants note that the claims are limited to the compositions themselves and not methods of using the compositions. The scope of enablement must be commensurate with the scope of the claimed invention and not all potential non-claimed uses of the invention.

Furthermore, spermicidal topical compositions and the use of such composition are also well known to those skilled in the art (see page 1, lines 28-31 and Page 11, line 30 through page 12, line 7). In accordance with one use of the present invention, applicants are simply conjugating a known anti-sperm agent to the claimed antibody and then using that complex as the active agent in a spermicidal composition, as has been done previously for many anti-sperm agents. Since the compositions are topical, the issue of establishing adequate concentration of the active agent at the desired site of activity is simply a matter of routine experimentation. Applicants respectfully submit they have taught how to make and use the claimed antibodies, and that the Examiner has failed to provide any reason to doubt the objective teachings of the present invention. Applicants respectfully submit the specification fully describes and enables the invention as claimed, and applicants request the withdrawal of the rejection of claims 5, 6, 13 and 14 under 35 USC § 112, first paragraph.

The application as amended is believed to be in condition for allowance and applicants hereby request the withdrawal of the rejections under 35 USC § 103, 35 USC § 112, first and second paragraphs and passage of the application to issuance. The Commissioner is hereby authorized to charge any fees due for this submission to Deposit Account No. 50-0423, as well as credit any refunds.

Respectfully submitted,



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Appendix A

S19 Heavy Chain

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GGGAATTCAT GGAATGGAGC TGGTTTTCCT CTTCTTGGTA GCAACAGCCT CAGGTGTCCAC '472 patent

TCCCAGGTC CAATTGCAGC AACCTGG_TC TGAACCGGTGA GGCCTGGAGC TTCAGTGAAG '472 patent
   CAGGTG AAACTGCAGC AACCTGGGTC TGAACCGGTGA GGCCTGGAGC TTCAGTGAAG  present

GTGTCCTGCA GGGCTTCTGG CTACAAATTC ACCACCTACT GGATGCACTG GGTGAGGCAG '472 patent
GTGTCCTGCA GGGCTTCTGG CTACAAATTC ACCACCTACT GGATGCACTG GGTGAGGCAG  present

AGGCCTGGAC AAGGCCCTGA GTGGATTGGA GATATTTATC CTGGTAGTGG TGATTCTAAC '472 patent
AGGCCTGGAC AAGGCCCTGA GTGGATTGGA GATATTTATC CTGGTAGTGG TGATTCTAAC  present

TACGATGTGA AGTTCAAGAA CAAGGCCACA CTGACTGTAG ACACATCCTC CAGCACAGTT '472 patent
TACGATGTGA AGTTCAAGAA CAAGGCCACA CTGACTGTAG ACACATCCTC CAGCACAGTT  present

TACATACAAC TCAGCAGCCT GACATCTGAG GACTCCGCGG TCTATTACTG TGCAAGAAGG '472 patent
TACATACAAC TCAGCAGCCT GACATCTGAG GACTCCGCGG TCTATTACTG TGCAAGAGGG  present

GACTATGGTT GCCCTTTTGT TTACTGGGGC CAAGGGACTC TGGTCACTGT CTCTGCAGCC '472 patent
GACTATGGTT GCCCTTTTGT TTACTGGGGC CAAGGCACCA CGGTCACCGT CTCCAGT     present

AAAACGACAC CCCCATCCGT TTATCCCCTG GCCCCTAGAA CTTGGG                 '472 patent
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S19 Light Chain

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GACATTGTGC TGACCCAATC TCCAGCTTCT CCCTGCCTGT CAGTCTTGGA GATCCAGCCT '472 patent
GACATCGAGC TCACTCAGTC TCCA  TTCT CCCTGCCTGT CAGTCTTGGA GGTCCAGCCT  present

CCATCTCTTG CAGATCTAGT CAGAGTCTTG TACGCAGAAA TAGAGACACC TATTTACATT '472 patent
CCATCTCTTG CAGATCTAGT CAGAGTCTTG TACACAGTAA TAGAGACACT TATTTACATT  present

GGTTCCTGCA GAAGCCAGGC CAGTCTCCAG AGCTCCTGAT CTACAGAGTT TCCAACCGAT '472 patent
GGTTCCTGCA GAAGCCAGGC CAGTCTCCAG AGCTCCTGAT CTACAGAGTT TCCAACCGAT  present

TTTCTGGGGT CCCAGACAGG TTCAGTGGCA GTGGATCAGG GACAGATTTC ACACTCAAGA '472 patent
TTTCTGGGGT CCCAGACAGG TTCAGTGGCA GTGGATCAGG GACAGATTTC ACACTCAAGA  present

TCAGCAGAGT GGAGGCTGAG GATCTGGGAG TTTATTTCTG TTCTCAAAGT ACACATGTTC '472 patent
TCAGCAGAGT GGAGGCTGAG GATCTGGGAG TTTATTTCTG TTCTCAAAGT ACACATGTTC  present

CATTCACGTT CGGCTCGGGG ACAAAGTTGG AAATAAAACG GGCTGATGCT GCACCAACTG '472 patent
CATTCACGTT CGGCTCGGGG ACCAAGCTGG AAATCAAACG GGCGGCCGCA             present
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